DEPARTMENT OF HEALTH & HUMAN SERVICES

Food end Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

Our STN: BL 103945/0

October 23, 2001

Pinya Cohen, Ph.D.
Nabi
5800 Park of Commerce Blvd., N.W.
Boca Raton, FL 33487

Dear Dr. Cohen:

Your Biologics License Application for Hepatitis B Immune Globulin (Human) [Nabi-HB™] to include treatment of acute exposure to HBsAg following acute exposure to blood containing HBsAg, perinatal exposure of infants born to HBsAg-positive mothers, sexual exposure to HBsAg-positive persons, and household exposure of infants to persons with acute hepatitis B virus infection, has been approved effective today. Nabi is hereby authorized to introduce or deliver for introduction into interstate commerce Hepatitis B Immune Globulin (Human), manufactured at Nabi under U.S. License No. 1022.

Under this license you are authorized to introduce or deliver for introduction into interstate commerce Hepatitis B Immune Globulin (Human) [Nabi-HB], as a sterile solution in three dosage forms: 1 mL in a 2 mL vial, 5 mL in a 6 mL vial, and 0.5 mL in a 1 mL syringe. The product potency is expressed in International Units (IU) by comparison to the World Health Organization (WHO) standard. Each vial contains greater than 3 12 IU/mL anti-HBs. The potency of each vial exceeds the potency of anti-HBs in an U.S. reference hepatitis B immune globulin (FDA). The U.S. reference has been tested by Nabi against the WHO standard and found to be equivalent to 208 IU/mL. For post-exposure prophylaxis, the product must be administered intramuscularly. Under this authorization, you are approved to manufacture Hepatitis B Immune Globulin (Human) at your, ——— 'facility, and filling and packaging at your ——— facility, ———, located in' ———. Changes to the product, production process, location of production process, equipment, facilities, or responsible personnel are required to be reported to FDA as specified in Title 21 Code of Federal Regulations (CFR) Section 601.12.

The dating period for this product shall be 24 months from the date of manufacture when stored at 2-8° C. The date of manufacture shall be defined as the date of the initial sterile filtration of the formulated bulk. Results of ongoing stability studies should be submitted throughout the dating period as they become available.

We note the post-approval commitments (PAC) regarding the filling facility: ——— ——— „ described in your letter dated August 15, 2001, submitted as an amendment to the Biologics License Application. While these PAC items are not under Section 506B of the Food, Drug and Cosmetic Act, information on the suggested format for submission

of any study reports to your licenses application may be found in the CBER Standard Operating Procedure and Policy document titled "Postmarketing Commitment Annual Reports. Final Reports, and Related Submission - Administrative Handling. Review. and CBER Reporting" (available at http://www.fda.gov/cber/regsopp/8413.htm). These PACs are:

1. To submit to your BLA the final study report for the bioburden study for Capping Room 115. We acknowledge the proposed study completion date, supplied by [redacted], of December 31, 2001.

2. To submit to your next annual report, notification of the completion of the installation and qualification of new [redacted] that will be used for [redacted]. This notification should be clearly segregated from the other annual report items and labeled to include a reference to the STN (s) applicable to this approval action.

In addition, we note the post-approval commitments described in your letters dated September 25, 2001 and October 16, 2001 submitted as amendments to the Biologics License Application.

1. To validate a [redacted] purity assay to characterize [redacted] observed in [redacted], solutions against known reference standards. A revision to SOP [redacted] should be submitted as soon as possible thereafter.

2. To complete the validation of the [redacted] assay as a back up potency assay. The validation will compare results using [redacted] to results using the [redacted] assay With [redacted] The validation study should be submitted as a Prior Approval Supplement.

All adverse reports should be submitted according to 21 CFR 600.80 to the Center for Biologics Evaluation and Research (CBER), HFM-210, Food and Drug Administration, 1401 Rockville Pike, Rockville, Maryland 20852-1448. In addition, safety related information obtained in the course of other relevant clinical studies should be reported in accordance with 21 CFR 3 12.32. It is also requested that distribution reports be submitted according to 2 1 CFR 600.8 1.

Please submit three (3) copies of final printed labeling at the time of use accompanied by Part II of FDA Form 2567 with completed implementation information. In addition, you may wish to submit your proposed introductory advertising and promotional campaign. If so, please submit three (3) copies of the proposed material in draft form with Part I of the FDA Form 2567/2253 to CBER, Advertising and Promotional Labeling Branch (APLB), HFM-602, 1401 Rockville Pike, Rockville, Maryland 20852-1448. Promotional claims should be consistent with and not contrary to the approved labeling. No comparative claims or claims of superiority over other similar products should be made

unless data to support such claims are submitted to and approved by CBER. Final copies of advertising and promotional materials should be submitted at the time of use with Part II of FDA Form 2567/2253 to APLB. Please include copies of the approved labeling with your proposed or final copy of advertising and promotional materials submitted to CBER.

The information has been placed in your biologics license file. It is recommended that a copy of this letter be available for review at the time of FDA inspections.

Sincerely yours,

Jay S. Epstein, M.D.
Director
Office of Blood Research and Review
Center for Biologics Evaluation
and Research

Steven A. Masiello
Director
Office of Compliance
and Biologics Quality
Center for Biologics Evaluation
and Research